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10/748,525	12/29/2003	Tae-Woong Koo	21058/0206735-US0	9348

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EXAMINER	
POHNERT, STEVEN C	
ART UNIT	PAPER NUMBER
1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/748,525	KOO ET AL.	
	Examiner	Art Unit	
	Steven C. Pohnert	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-25 and 28-38* is/are pending in the application.

4a) Of the above claim(s) *11-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-10,24,25 and 28-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

This action is in response to papers filed 12/27/2007.

The 112-1st paragraph enablement rejection of claims 3 and 26 is withdrawn as the claims have been canceled.

Claims 11-23 have been withdrawn from consideration as drawn to a non-elected invention in the response to restriction of 7/10/2006.

Claims 35-38 have been added by amendment.

Claims 1-2, 5-10, 24-25, 28-38 are being examined.

This action is FINAL.

Maintained and New Grounds of Rejection necessitated by amendment.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 35 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claims 35 and 36 added by amendment depends from claims 1 and 24 and require, “wherein a location of a peak in a response spectra…” in the first two lines. Claims 1 and 24 do not teach or recite a peak location or a spectra. It is thus unclear to what location or peak the claims are referring. Further claims 35 and 36 added by amendment recites the limitation "the number of the particular labeled oligonucleotide probe" in the last line. Claims 35 and 36 depend from claims 1 and 24 respectively.

Neither claims 1 or 24 recite "a number of particular labeled oligonucleotide probe." There is insufficient antecedent basis for this limitation in the claim. For art purposes the claims will be interpreted to be drawn to the number of signal molecules of a particular labeled oligonucleotide probe.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1-2, 5, 7-9, 24-25, 28, 31, 32, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Cronin et al (US patent 6,045,996, issued April 4, 2000).

With regards to claim 1, Cronin teaches an array of at least 500 different oligonucleotide features per square centimeter at discrete locations (see column 2, lines 23-27). These 500 oligonucleotides are a population of labeled oligonucleotide probes. Cronin further teaches labeling a target with luminescent dyes including polymethine dyes (see column 6, lines 12-22). Cronin further allowing hybridization and determining the identity of the probes to which they are labeled. The hybridization is labeling a probe. Cronin exemplifies this in the example. Cronin's hybridized array is a population of labeled oligonucleotides, comprising an oligonucleotide associated with the detectably distinguishable signal molecules (each labeled molecule is hybridized to a probe at a discrete location), the type and number of signaling molecules is less than

the number of probes. As the nucleic acid sequence and location of the probes of Cronin's array are known, the detection of the label allows identification of the type of nucleotide at each position.

With regards to claim 2, Cronin teaches the target can be labeled at one nucleotide (see column 6 line 12). Cronin thus teaches the label is present once, which is less than 4 times.

The specification does not specifically define a reference signal molecule, but teaches an exemplary list in table 1, page 11.

With regards to claim 5, Cronin teaches fluorescein as a label. This is listed in the specification as an exemplary reference signal molecule. Cronin thus teaches probes labeled with reference intensity molecules.

With regards to claim 7 and 8, Cronin teaches the use of polymethine dyes, fluorescien, rhodamine, and so forth (column 6, lines 20-22). Cronin further teaches the use of Cy3 and Cy5 (see column 9, line 17). Cronin thus teaches oligonucleotide probes labeled with Raman labels, polymethine dyes and signal molecules from table 1.

With regards to claim 9, Cronin et al teaches the fluorescien, rhodamine, CY3, and Cy5 labels (see column 6, lines 20-22; column 9, line 17). Cronin thus teaches fluorescent dyes.

With regards to claim 24, Cronin teaches an array of at least 500 different oligonucleotide features per square centimeter at discrete locations (see column 2, lines 23-27). These 500 oligonucleotides are a population of labeled oligonucleotide probes. Cronin further teaches labeling a target with luminescent dyes including polymethine

dyes (see column 6, lines 12-22). Cronin further teaches allowing hybridization of the capture probe and target nucleotide and determining the identity of the probes to which they are labeled. The hybridization is labeling a probe. Cronin exemplifies this in the example. Cronin's hybridized array is a population of labeled oligonucleotides, comprising an oligonucleotide associated with the detectably distinguishable signal molecules (each labeled molecule is hybridized to a probe at a discrete location), the type and number of signaling molecules is less than the number of probes. As the nucleic acid sequence and location of the probes of Cronin's array are known, the detection of the label allows identification of the type of nucleotide at each position.

With regards to claim 25, Cronin teaches the target can be labeled at one nucleotide (see column 6 line 12). Cronin thus teaches the label is present one, which is less than 4 times.

The specification does not specifically define a reference signal molecule, but teaches an exemplary list in table 1, page 11.

With regards to claim 28, Cronin teaches the fluorescein as a label. This is listed in the specification as an exemplary reference signal molecule. Cronin thus teaches probes labeled with reference intensity molecules.

With regards to claim 31 and 32, Cronin teaches the use of polymethine dyes, fluorescien, rhodamine, and so forth (column 6, lines 20-22). Cronin further teaches the use of Cy3 and Cy5 (see column 9, line 17). Cronin thus teaches oligonucleotide probes labeled with Raman labels, polymethine dyes and signal molecules from table 1.

With regards to claim 33, Cronin et al teaches the fluorescien, rhodamine CY3, and Cy5 labels (see column 6, lines 20-22; column 9, line 17). Cronin thus teaches fluorescent dyes.

Response to arguments

6. The response asserts that the Cronin does not anticipate the instant claims, as the instant claims require the labeled probes are identified by intensity. The claims are drawn to a composition, and compositions are defined by structural limitations. The art of Cronin teaches the structural limitations of the claims and thus anticipates the claims. The arguments to the functional limitations of the oligonucleotide probes, are moot as they are not directed to the structure of the compositions as claimed. The rejection is thus maintained.

7. Claim 1, 2, 5-10, 24, 25, 28-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Han et al (Nature Biotechnology (2001) volume 19, pages 631-635).

Newly added claims 35-38 have been added to this rejection.

Han et al teaches a method of using multicolor optical coding for biological assays. Han teaches the use of 6 colors and 10 intensities could code for 1 million nucleic acid sequences (see abstract).

With regards to claim 1, Han further teaches the use of 3 colors and 10-intensities results in 999 codes (see page 631, 2nd column, 1st full paragraph). Han teaches in figure 5, 4 probes that are labeled with 3 different colors, which can be used to identify a nucleotide sequence.

With regards to claim 2, Han teaches in figure 5, the use of each label only once.

With regards to claim 5, Han et al teaches each labeled oligonucleotide probe is labeled with F by binding of the target nucleic acid (see figure 5).

With regards to claim 6, Han teaches probes of the same length, namely 14 nucleotides, in figure 5 which are from 10 to 50 nucleotides.

With regards to claim 7 and 8, Han teaches the use of adenine in the probes, represented by an A in the nucleotide sequences (see figure 6 and legend). As claim 8 depends from claim 7, the claims teach that adenine is a Raman label. Thus Han teaches Raman labels and signal molecules from table 1.

With regards to claim 9, Han et al teaches the use of quantum dots (see abstract).

With regards to claim 10, Han teaches the use of quantum dots, which are "zinc sulfide-capped cadmium selenide nanocrystals" (see abstract 2nd line). Han thus teaches the use of nanotags.

With regards to claim 24, Han further teaches the use of 3 colors and 10-intensities results in 999 codes (see page 631, 2nd column, 1st full paragraph). Han teaches in figure 5, 4 probes that are labeled with 3 different colors, which can be used to identify a nucleotide sequence. Han further teaches the labeled probes are hybridized to a complementary strand and are thus a reaction mixture.

With regards to claim 25, Han teaches in figure 5, the use of each label only once. Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each signal molecule is present once.

With regards to claim 28, Han et al teaches each labeled oligonucleotide probe is labeled with F by binding of the target nucleic acid (see figure 5). Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each signal molecule has an intensity reference signal.

With regards to claim 29 and 30, Han teaches probes of the same length in figure 5 and are from 10 to 50 nucleotides. Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each oligonucleotide is identical in length (claims 29 and 30) and length of 10 to 50 nucleotides.

With regards to claim 31 and 32, Han teaches the use of adenine in the probes, represented by an A in the nucleotide sequences (see figure 6 and legend). As claim 32 depends from claim 31, the claims teach that adenine is a Raman label. Thus Han teaches Raman labels and signal molecules from table 1. Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each signal molecule is a Raman label or signal molecule from table 1.

With regards to claim 33, Han et al teaches the use of quantum dots (see abstract). Han thus teaches a reaction mixture with a target polynucleotide and a labeled probe, wherein each signal molecule is a quantum dot.

With regards to claim 34, Han teaches the use of quantum dots, which are “zinc sulfide-capped cadmium selenide nanocrystals” (see abstract 2nd line). Han thus teaches the use of nanotags.

Claims 35 and 36 require the size of the peak is proportional to the number of the particular labeled oligonucleotide pair. This is being broadly interpreted as the size of the peak is proportional to the number of signal molecules.

With regards to claims 35 and 36, Han teaches the size of the peaks is proportional to the number of the signaling molecules in each bead (see figure 1). Han thus teaches the size of the peaks is proportional to the number of labeled signal molecules.

The specification does not set forth a limiting definition of a subunit. Subunit is thus being given the broadest reasonable interpretation as a probe.

With regards to claims 37 and 38, Han teaches the use of beads of 6 colors and 10 intensities could code for 1 million nucleic acid sequences (see abstract). Han further teaches the use of 3 colors and 10-intensities results in 999 codes (see page 631, 2nd column, 1st full paragraph). Han teaches in figure 5, 4 probes that are labeled with 3 different colors, which can be used to identify a nucleotide sequence. Each bead is a signal molecule and thus the bead encodes a subunit of a template polynucleotide.

Response to arguments

The response asserts that the Han does not anticipate the instant claims, as the instant claims require the labeled probes are identified by intensity. . The claims are drawn to a composition, and compositions are defined by structural limitations. The art of Han teaches the structural limitations of the claims and thus anticipates the claims. The arguments to the functional limitations of the oligonucleotide probes, are moot as they are not directed to the structure of the compositions as claimed. The rejection is

thus maintained. The response further asserts, "Han teaches a method of DNA sequencing based on detection and identification of single fluorescently labeled mononucleotide molecules degraded from DNA strands in a cone shaped microcapillary. (Abstract)" However, Han teaches, "Multicolor optical coding for biological assays has been achieved by embedding different-sized quantum dots (zinc sulfide-capped cadmium selenide nanocrystals) into polymeric microbeads at precisely controlled ratios. Their novel optical properties (e.g., size-tunable emission and simultaneous excitation) render these highly luminescent quantum dots (QDs) ideal fluorophores for wavelength-and-intensity multiplexing. The use of 10 intensity levels and 6 colors could theoretically code one million nucleic acid or protein sequences. Imaging and spectroscopic measurements indicate that the QD-tagged beads are highly uniform and reproducible, yielding bead identification accuracies as high as 99.99% under favorable conditions. DNA hybridization studies demonstrate that the coding and target signals can be simultaneously read at the single-bead level. This spectral coding technology is expected to open new opportunities in gene expression studies, high-throughput screening, and medical diagnostics" (see abstract). Thus Han does not teach sequencing by degradation, but hybridization with labeled probes and identification by intensity.

Further Han teaches in figure 1 A, identification by intensity. Thus Han does teach identification of a nucleic acid by intensity as the claim requires and the rejection is maintained.

8. Claims 1-3 and 24-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Lockhart et al (WO97/27317, published July 31, 1997).

. The claims are drawn to a composition, and compositions are defined by structural limitations. With regards to claim 1, Lockhart et al teaches in figure 24, probe 1 ACTG and probe CTGT. Lockhart thus teaches an isolated population of labeled oligonucleotides associated with detectably distinguishable labels, wherein the type of each nucleotide at each position is identified by an intensity of at least one label.

With regards to claim 2, Lockhart teaches al teaches in figure 24, probe 1 ACTG and probe 2 CTGT. Each label occurs less than 4 times per labeled nucleotide.

With regards to claim 3, probes 1 and 2 of Lockhart each comprise 4 nucleotides, thus the number of unique sequences is equal to the number of nucleotides of the labeled oligonucleotide probes.

With regards to claim 24, Lockhart et al teaches in figure 24, probe 1 ACTG and probe CTGT. Lockhart teaches hybridization or target nucleic acids to arrays. Lockhart thus teaches a reaction mixture comprising isolated population of labeled oligonucleotides associated with detectably distinguishable labels, wherein the type of each nucleotide at each position is identified by an intensity of at least one label.

With regards to claim 25, Lockhart teaches al teaches in figure 24, probe 1 ACTG and probe 2 CTGT. Each label occurs less than 4 times per labeled nucleotide.

With regards to claim 26, probes 1 and 2 of Lockhart each comprise 4 nucleotides, thus the number of unique sequences is equal to the number of nucleotides of the labeled oligonucleotide probes.

Response to arguments

The response asserts that the Lockhart does not anticipate the instant claims, as the instant claims require the labeled probes are identified by intensity. . The claims are drawn to a composition, and compositions are defined by structural limitations. The art of Lockhart teaches the structural limitations of the claims and thus anticipates the claims. The arguments to the functional limitations of the oligonucleotide probes, are moot as they are not directed to the structure of the compositions as claimed. The rejection is thus maintained. Lockhart thus anticipates the claims and the rejections are maintained.

Summary

NO claims are allowed over prior art cited.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Steven C. Pohnert whose telephone number is 571-272-3803. The examiner can normally be reached on Monday-Friday 6:30-4:00, second Friday off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ram Shukla can be reached on 571-272-0735. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Steven Pohnert

/Ram R. Shukla/
Supervisory Patent Examiner, Art Unit 1634